

PATENT

Customer No. 22,852

Customer No. 22,852

Attorney Docket No. 08702.0009-01000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

LEONARD et al.

Application No.: 09/512,701

Filed: February 25, 2000

For: USE OF IL-12 ANTAGONISTS IN
THE TREATMENT OF
RHEUMATOID ARTHRITIS

Group Art Unit: 1645

Examiner: N. M. Minnifield

Commissioner for Patents
Washington, DC 20231

Sir:

INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R. § 1.97(c)

Pursuant to 37 C.F.R. §§ 1.56 and 1.97(c), Applicants bring to the attention of the Examiner the documents listed on the attached PTO 1449. This Information Disclosure Statement is being filed after the events recited in Section 1.97(b) but, to the undersigned's knowledge, before the mailing date of either a Final action, Quayle action, or a Notice of Allowance. Under the provisions of 37 C.F.R. § 1.97(c), this Information Disclosure Statement is accompanied by a fee of \$180.00 as specified by Section 1.17(p).

Copies of the listed documents are enclosed. Applicants respectfully request that the Examiner consider the listed documents and indicate that they were considered by making appropriate notations on the attached form.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that each or all of the listed documents are material or constitute "prior art." If the Examiner applies any of the documents as prior art against any claims in the application and Applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the office the relevant facts and law regarding the appropriate status of such documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should one or more of the documents be applied against the claims of the present application.

If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

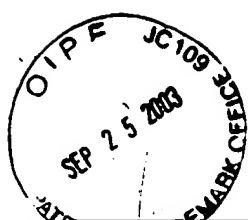
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: February 26, 2003

By: Rebecca M. McNeill
Rebecca M. McNeill
Reg. No. 43,796

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com



INFORMATION DISCLOSURE CITATION

COPY RECEIVED
 OMB No. 0651-0011
 OCT 01 2003
 TECH CENTER 1600/2900

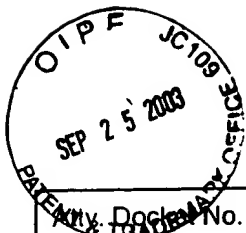
Atty. Docket No.	08702.0009-01000	Appln. No.	09/512,701
Applicant	LEONARD et al.		
Filing Date	February 25, 2000	Group:	1645

U.S. PATENT DOCUMENTS

Examiner Initial*	Document Number	Issue Date	Name	Class	Sub Class	Filing Date If Appropriate
	5,536,657	16 Jul. 1996	Chua et al.			
	5,650,492	22 Jul. 1997	Gately et al.			
	5,840,530	24 Nov. 1998	Gubler et al.			
	5,852,176	22 Dec. 1998	Gubler et al.			
	5,853,721	29 Dec. 1998	Gately et al.			
	5,955,476	21 Sep. 1999	Muller et al.			
	5,969,102	19 Oct. 1999	Bram et al.			
	6,054,487	25 Apr. 2000	Sekut et al.			
	6,225,117 B1	1 May 2001	Gately et al.			
	6,258,562 B1	10 Jul. 2001	Salfeld et al.			
	6,338,848 B1	15 Jan. 2002	Leonard et al.			

FOREIGN PATENT DOCUMENTS

Document Number	Publication Date	Country	Class	Sub Class	Translation Yes or N
WO 92/05256	02 Apr. 1992	WIPO			
WO 93/19770	14 Oct. 1993	WIPO			
WO 98/16248	23 Apr. 1998	WIPO			
WO 98/22137	28 May 1998	WIPO			
WO 98/41232	24 Sep. 1998	WIPO			
WO 99/36073	22 Jul. 1999	WIPO			
WO 99/37682	29 Jul. 1999	WIPO			
0 433 827 A2	26 Jun. 1991	EPO			



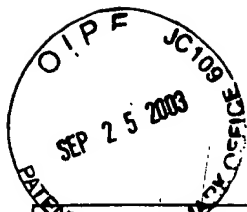
OMB No. 0651-0011

INFORMATION DISCLOSURE CITATION

RECEIVED
OCT 01 2003
TECH CENTER 1600/2900

Appn. No.	08702.0009-01000	Appln. No.	09/512,701
Applicant	LEONARD et al.		
Filing Date	February 25, 2000	Group:	1645

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)	
	Arnaudova et al., Application of Interferon- γ Containing Gel for Local Treatment of Skin Ulcers in Autoimmune Vasculitides and Skin Changes in Progressive Systemic Sclerosis, <i>The Journal of Rheumatology</i> , 20:1445-1446 (1993).
	Bach, Immunosuppressive Therapy of Autoimmune Diseases, <i>Immunology Today</i> , 14:322-326 (1993).
	Bach, Immunosuppressive Therapy of Autoimmune Diseases, <i>Trends in Pharmacological Sciences</i> , 14:213-216 (1993).
	Balashov et al., Increased Interleukin 12 Production in Progressive Multiple Sclerosis: Induction by Activated CD4 ⁺ T Cells Via CD40 Ligand, <i>Proceedings of the National Academy of Sciences U.S.A.</i> , 94:599-603 (1997).
	Bankhurst, Interferons and Systemic Lupus Erythematosus, <i>Journal of Rheumatology</i> , 14:63-67 (1987).
	Baron et al., Production of Tumor Necrosis Factor and Other Proinflammatory Cytokines by Human Mononuclear Phagocytes Stimulated with Myelin P2 Protein, <i>Proceedings of the National Academy of Sciences U.S.A.</i> , 90:4414-4418 (1993).
	Baron et al., Surface Expression of $\alpha 4$ Integrin by CD4 T Cells is Required for Their Entry into Brain Parenchyma, <i>Journal of Experimental Medicine</i> , 177:57-68 (1993).
	Butler et al., Anti-IL-12 and Anti-TNF Antibodies Synergistically Suppress the Progression of Murine Collagen-Induced Arthritis, <i>European Journal of Immunology</i> , 29:2205-2212 (1999).
	Campbell et al., Essential Role for Interferon- γ and Interleukin-6 in Autoimmune Insulin-Dependent Diabetes in NOD/Wehi Mice, <i>Journal of Clinical Investigation</i> , 87:739-742 (1991).
	Castaño et al., Type-I Diabetes: A Chronic Autoimmune Disease of Human, Mouse, and Rat, <i>Annual Review of Immunology</i> , 8:647-679 (1990).
	Chan et al., Induction of Interferon γ Production by Natural Killer Cell Stimulatory Factor: Characterization of the Responder Cells and Synergy with Other Inducers, <i>Journal of Experimental Medicine</i> , 173:869-879 (1991).
	Charteris et al., Interferon-Gamma (IFN- γ) Production <i>In Vivo</i> in Experimental Autoimmune Uveoretinitis, <i>Immunology</i> , 75:463-467 (1992).
	Chizzonite et al., IL-12 Receptor. I. Characterization of the Receptor on Phytohemagglutinin-Activated Human Lymphoblasts, <i>The Journal of Immunology</i> , 148:3117-3124 (1992).
	Chizzonite et al., IL-12: Monoclonal Antibodies Specific for the 40-kDa Subunit Block Receptor Binding and Biologic Activity on Activated Human Lymphoblasts, <i>The Journal of Immunology</i> , 147:1548-1556 (1991).
	Chofflon et al., Tumor Necrosis Factor α Production as a Possible Predictor of Relapse in Patients with Multiple Sclerosis, <i>European Cytokine Network</i> , 3:523-531 (1992).

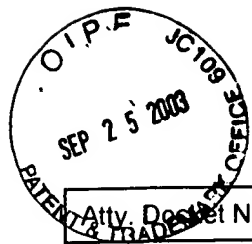


INFORMATION DISCLOSURE CITATION

OMB No. 0651-0011
RECEIVED
 OCT 01 2003
 TECH CENTER 1600/2900

App. No.	08702.0009-01000	Appln. No.	09/512,701
Applicant	LEONARD et al.		
Filing Date	February 25, 2000	Group:	1645

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)	
	Chua et al., Expression Cloning of a Human IL-12 Receptor Component: A New Member of the Cytokine Receptor Superfamily with Strong Homology to gp130, <i>The Journal of Immunology</i> , 153:128-136 (1994).
	Constantinescu et al., IL-12 Reverses the Suppressive Effect of the CD40 Ligand Blockade on Experimental Autoimmune Encephalomyelitis (EAE), <i>Journal of the Neurological Sciences</i> , 171:60-64 (1999).
	Deguchi et al., Tumour Necrosis Factor/Cachectin Plays a Key Role in Autoimmune Pulmonary Inflammation in Lupus-Prone Mice, <i>Clinical and Experimental Immunology</i> , 85:392-395 (1991).
	Duchmann et al., Interleukin-12 mRNA is Induced in Lamina Propria Mononuclear Cells from Patients with Inflammatory Bowel Disease (IBD), <i>Gastroenterology (Suppl.)</i> , 104:A693 (1993).
	Feldmann et al., Evaluation of the Role of Cytokines in Autoimmune Disease: The Importance of TNF α in Rheumatoid Arthritis, <i>Progress in Growth Factor Research</i> , 4:247-255 (1992).
	Fox et al., Anti-Interleukin-12 Antibody: Potential Role in Preventing Relapses of Multiple Sclerosis, <i>BioDrugs</i> , 13:233-241 (2000).
	Fujihira et al., Suppression and Acceleration of Autoimmune Diabetes by Neutralization of Endogenous Interleukin-12 in NOD Mice, <i>Diabetes</i> , 49:1998-2006 (2000).
	Funauchi et al., Serum Level of Interferon- γ in Autoimmune Diseases, <i>Tohoku Journal of Experimental Medicine</i> , 164:259-267 (1991).
	Gately et al., Interleukin-12 Antagonist Activity of Mouse Interleukin-12 p40 Homodimer <i>in Vitro</i> and <i>in Vivo</i> , <i>Annals New York Academy of Sciences</i> , 795:1-12 (1996).
	Germann et al., IL-12, a Cytokine with Multiple Effects on T _H 1-, but not on T _H 2-cells, <i>Immunobiology</i> , 186:38 (1992).
	Godfrey et al., A Developmental Pathway Involving Four Phenotypically and Functionally Distinct Subsets of CD3 ⁺ CD4 ⁺ CD8 ⁻ Triple-Negative Adult Mouse Thymocytes Defined by CD44 and CD25 Expression, <i>The Journal of Immunology</i> , 150:4244-4252 (1993).
	Greig et al., A Comparison of the Effects of Melengestrol Acetate and Hydrocortisone Acetate on Experimental Allergic Encephalomyelitis in Rats, <i>The Journal of Pharmacology and Experimental Therapeutics</i> , 173:85-93 (1970).
	Harris, et al., Therapeutic Antibodies - The Coming of Age, <i>Trends in Biotechnology</i> , 11:42-44 (1993).
	Heremans et al., Role of Endogenous Interleukin-12 (IL-12) in Induced and Spontaneous Relapses of Experimental Autoimmune Encephalomyelitis in Mice, <i>European Cytokine Network</i> , 10:171-179 (1999).
	Higgins et al., Suppression of Experimental Autoimmune Encephalomyelitis by Oral Administration of Myelin Basic Protein and Its Fragments, <i>The Journal of Immunology</i> , 140:440-445 (1988).
	Hofman et al., Immunoregulatory Molecules and IL 2 Receptors Identified in Multiple Sclerosis Brain, <i>The Journal of Immunology</i> , 136:3239-3245 (1986).



INFORMATION DISCLOSURE CITATION

Attv. Designet No.	08702.0009-01000	Appln. No.	09/512,701
Applicant	LEONARD et al.		
Filing Date	February 25, 2000	Group:	1645

RECEIVED
OCT 01 2003
TECH CENTER 1600/2900

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)	
	Hofman et al., Lymphokines and Immunoregulatory Molecules in Subacute Sclerosing Panencephalitis, <i>Clinical Immunology and Immunopathology</i> , 58:331-342 (1991).
	Hofman et al., Tumor Necrosis Factor Identified in Multiple Sclerosis Brain, <i>Journal of Experimental Medicine</i> , 170:607-612 (1989).
	Hunter et al., Immunoregulation by Interleukin-12 in MB49.1 Tumor-Bearing Mice: Cellular and Cytokine-Mediated Effector Mechanisms, <i>European Journal of Immunology</i> , 27:3438-3446 (1997).
	Ichikawa et al., Anti-IL-12 Antibody Prevents the Development and Progression of Multiple Sclerosis-Like Relapsing-Remitting Demyelinating Disease in NOD Mice Induced with Myelin Oligodendrocyte Glycoprotein Peptide, <i>Journal of Neuroimmunology</i> , 102:56-66 (2000).
	Jaffe, Combination Therapy of Rheumatoid Arthritis—Rationale and Overview, <i>Journal of Rheumatology</i> , 17 (supplement 25): 24-27 (1990).
	Joosten et al., Blockade of endogenous interleukin 12 results in suppression of murine streptococcal cell wall arthritis by enhancement of interleukin 10 and interleukin 1Ra, <i>Annals of Rheumatic Diseases</i> , 59(3): 196-205 (2000).
	Karlsson et al., Autoimmune Endocrinopathies 5: Autoimmune Disease of the Adrenal Cortex, Pituitary, Parathyroid Glands and Gastric Mucosa, <i>Journal of Internal Medicine</i> , 234:379-386 (1993).
	Kim et al., The role of IL-12 in Inflammatory Activity of Patients with Rheumatoid Arthritis (RA), <i>Clinical and Experimental Immunology</i> , 119:175-181 (2000).
	Kobayashi et al., Identification and Purification of Natural Killer Cell Stimulatory Factor (NKSF), a Cytokine with Multiple Biologic Effects on Human Lymphocytes, <i>Journal of Experimental Medicine</i> , 170:827-845 (1989).
	Lagoo et al., Proinflammatory Cytokine Production by Rheumatoid Arthritis Synovial Fibroblasts, <i>Journal of Cellular Biochemistry (Suppl. O)</i> , 17:146 (1993).
	Leonard et al., Effects of Single-Dose Interleukin-12 Exposure on Interleukin-12-Associated Toxicity and Interferon- γ Production, <i>Blood</i> , 90:2541-2548 (1997).
	Leonard et al., Prevention of Experimental Autoimmune Encephalomyelitis by Antibodies Against Interleukin 12, <i>Journal of Experimental Medicine</i> , 181:381-386 (1995).
	Leonard et al., Regulation of Experimental Autoimmune Encephalomyelitis by Interleukin-12, <i>Annals New York Academy of Sciences</i> , 795:216-226 (1996).
	Leonard et al., Regulation of the Inflammatory Response in Animal Models of Multiple Sclerosis by Interleukin-12, <i>Critical Reviews in Immunology</i> , 17:545-553 (1997).
	Lernmark et al., Autoimmune Endocrinopathies 3: Islet Cell Autoimmunity, <i>Journal of Internal Medicine</i> , 234:361-369 (1993).
	Malfait et al., Blockade of IL-12 During the Induction of Collagen-Induced Arthritis (CIA) Markedly Attenuates the Severity of the Arthritis, <i>Clinical and Experimental Immunology</i> , 111:377-383 (1998).

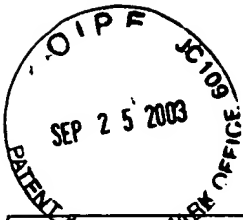


INFORMATION DISCLOSURE CITATION

Atty. Docket No. 08702.0009-01000	Appln. No. 09/512,701
Applicant LEONARD et al.	
Filing Date February 25, 2000	Group: 1645

RECEIVED
OCT 01 2003
TECH CENTER 1600/2900

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)	
	Manetti et al., Natural Killer Cell Stimulatory Factor (Interleukin 12 [IL-12]) Induces T Helper Type 1 (Th1)-Specific Immune Responses and Inhibits the Development of IL-4-Producing Th Cells., <i>Journal of Experimental Medicine</i> , 177:1199-1204 (1993).
	Merrill et al., Inflammatory Leukocytes and Cytokines in the Peptide-Induced Disease of Experimental Allergic Encephalomyelitis in SJL and B10.PL Mice, <i>Proceedings of the National Academy of Sciences U.S.A.</i> , 89:574-578 (1992).
	Merrill et al., T Cell Lines Established from Multiple Sclerosis Cerebrospinal Fluid T cells Using Human Retroviruses, <i>Journal of Neuroimmunology</i> , 21:213-226 (1989).
	Panitch et al., Treatment of Multiple Sclerosis with Gamma Interferon: Exacerbations Associated with Activation of the Immune System, <i>Neurology</i> , 37:1097-1102 (1987).
	Peeva et al., Rheumatoid Arthritis Exacerbation Caused by Exogenous Interleukin-12, <i>Arthritis & Rheumatism</i> , 43:461-463 (2000).
	Rothe et al., Suppression of Cyclophosphamide Induced Diabetes Development and Pancreatic Th1 Reactivity in NOD Mice Treated with the Interleukin (IL)-12 Antagonist IL-12(p40) ₂ , <i>Diabetologia</i> , 40:641-646 (1997).
	Saito et al., Effect of CD80 and CD86 Blockade and Anti-Interleukin-12 Treatment on Mouse Acute Graft-Versus-Host Disease, <i>European Journal of Immunology</i> , 26:3098-3106 (1996).
	Serreze, Autoimmune diabetes results from genetic defects manifest by antigen presenting cells, <i>FASEB Journal</i> , 7:1092-1096 (1993).
	Simon et al., Divergent T-cell Cytokine Patterns in Inflammatory Arthritis, <i>Proceedings of the National Academy of Sciences U.S.A.</i> , 91:8562-8566 (1994).
	Smith et al., Interleukin-12 Induces Relapse in Experimental Allergic Encephalomyelitis in the Lewis Rat, <i>American Journal of Pathology</i> , 150:1909-1917 (1997).
	Smith et al., The Role of T Cells in Myosin-Induced Autoimmune Myocarditis, <i>Clinical Immunology and Immunopathology</i> , 68:100-106 (1993).
	Steinman, Autoimmune Disease: Misguided Assaults on the Self Produce Multiple Sclerosis, Juvenile Diabetes and Other Chronic Illnesses: Promising Therapies are Emerging, <i>Scientific American</i> , September:107-114 (1993).
	Tang, et al., The Effects of a Monoclonal Antibody to Interferon- γ on Experimental Autoimmune Thyroiditis (EAT): Prevention of Disease and Decrease of EAT-Specific T Cells, <i>European Journal of Immunology</i> , 23:275-278 (1993).
	Trinchieri et al., Natural Killer Cell Stimulatory Factor (NKSF) or Interleukin-12 is a Key Regulator of Immune Response and Inflammation, <i>Progress in Growth Factor Research</i> , 4:355-368 (1992).
	Van der Veen et al., The Effect of Methylprednisone Pulse Therapy on Methyldtrexate Treatment of Rheumatoid Arthritis, <i>Clinical Rheumatology</i> , 12:500-505 (1993).
	Veys et al., Interferon Gamma in Rheumatoid Arthritis - A Double Blind Study Comparing Human Recombinant Interferon Gamma with Placebo, <i>The Journal of Rheumatology</i> , 15:570-574 (1988).



OMB N . 0651-0011

INFORMATION DISCLOSURE CITATION

Atty. Docket No.	08702.0009-01000	Appln. No.	09/512,701
Applicant	LEONARD et al.		
Filing Date	February 25, 2000	Group:	1645

RECEIVED
OCT 01 2003
TECH CENTER 1600/2900

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Via et al., IL12 Prevents Autoimmunity in a Murine Model of SLE., <i>Arthritis and Rheumatism</i> , 36:148 (1993).
	Vitali, et al., Immunotherapy in Rheumatoid Arthritis, <i>The International Journal of Artificial Organs</i> , 16:196-200 (1993).
	Waldburger et al., Adoptive Transfer of Experimental Allergic Encephalomyelitis After <i>in Vitro</i> Treatment with Recombinant Murine Interleukin-12, <i>American Journal of Pathology</i> , 148:375-382 (1996).
	Wilske, Approaches to the Management of Rheumatoid Arthritis: Rationale for Early Combination Therapy, <i>British Journal of Rheumatology</i> , 32 (supplement 1) 24-27 (1993).

Examiner	Date Considered
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	
Form PTO 1449	Patent and Trademark Office - U.S. Department of Commerce



RECEIVED
OCT 01 2003
TECH CENTER 1600/2900

COPY

RDB/RMM/GWC

PLEASE STAMP TO ACKNOWLEDGE RECEIPT OF THE FOLLOWING:

In Re Application of: J. LEONARD et al.

Application No.: 09/512,701

Group Art Unit: 1645

Filed: February 25, 2000

Examiner: N. M. Minnifield

FOR: USE OF IL-12 ANTAGONISTS IN THE TREATMENT OF
RHEUMATOID ARTHRITIS

-
1. Information Disclosure Statement
 2. Form PTO-1449 with 86 documents listed therein

Dated: February 26, 2003

Docket No.: 8702.0009-01

RMM/JGB/cob - MailDrop 731



OK'd INC
2-27-0